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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,594	08/19/2003	Tony N. Frudakis	DNA1170-2	6207

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EXAMINER	
WHALEY, PABLO S	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,594	FRUDAKIS ET AL.	
	Examiner	Art Unit	
	PABLO WHALEY	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 84-115* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 84-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 07/02/2010, have been fully considered.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Applicant has not amended any claims in the response filed 07/02/2010, which has been entered and acknowledged. Applicant has cancelled claims 2-83.

Claims 1 and 84-115 are pending and under consideration.

Claim rejections - 35 USC § 112, 1st Paragraph

Response to Arguments

Applicant's arguments, filed 07/02/2010, that the paragraph [0330] of the published application (U.S. Pub. No. 2004/0229231) stating that "...most of the SNPs identified herein are non-coding, either silent polymorphisms or residing in the gene proximal promoter, intron or 3'UTR" provides support for SNPs not located in a gene encoding region are persuasive. Therefore the new matter rejection is withdrawn.

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, filed 07/02/2010, have been fully considered but are not persuasive for the following reasons.

In response to applicant's argument that Parra does not teach a second population of SNPs that is not located within a gene encoding region, and that Cargill

does not remedy this deficiency, the examiner maintains that Parra suggest more than one population of SNP [p.20, Col. 1, and Table 1, p.21, Col. 1, ¶ 2, and Fig. 1], and that Cargill teaches populations of non-coding SNPs [See e.g. Abstract, p.232-233, Results, Table 1, and Table 2], which makes obvious a second population of SNPs not located within a coding region of a gene.

In response to applicants' arguments that Sorenson and Pritchard also do not teach a second population of SNPs that is not located within a gene encoding region, these references were not cited as a teaching for this limitation, as discussed above.

For these reasons, the examiner maintains that the combination of references teaches and/or makes obvious the claimed limitations. Accordingly, the following rejections are maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35

U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 84-86, 90-97, 99-100, and 104-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parra et al. (Am. J. Physical Antropol., January 2001, Vol. 114, Issue 1, p. 18-29), in view of Cargill et al. (Nature Genetics, 1999, Vol. 22, p.231-238).

The amended claims are now drawn to a method of inferring, with a predetermined level of confidence, proportional ancestry of at least two ancestral groups of a test individual by identification of a population structure comprising: a) determining single nucleotide polymorphisms (SNPs) for a first population and identifying a first population of SNPs having a frequency differential (delta) > 0.4 between one or more pairs of population groups wherein the first population of SNPs are identified from a database in silico; b) contacting a parental sample nucleic acid with one or more hybridizing nucleic acids corresponding the first population of SNPs, wherein the one or more hybridizing nucleic acids selectively hybridize to the nucleic acid in the parental sample; c) selecting SNPs hybridizing in step (b) to generate a

second population of SNPs which have a minor allele frequency > 1% and (delta) > 0.4 for at least one pair of the at least two population groups, wherein at least one of the second population of SNPs is a SNP which may be correlated with but not linked to a gene-linked trait, wherein the second population of SNPs is an autosomal marker, and wherein the at least one SNP of the second population of SNPs is not located within a region of a gene encoding a protein; d) contacting a sample comprising nucleic acid molecules of a test individual with at least 20 second population of SNPs, wherein the second population of SNPs are indicative of a population structure, and wherein the population structure is correlated with a trait of the test individual; e) determining the nucleotide occurrences of the second population of SNPs in the sample from the test individual; and f) identifying the population structure indicated by the nucleotide occurrences determined for the test individual, wherein identifying the population structure infers the proportional ancestry of the test individual; and g) providing information resulting from steps (a) through (f) to a user.

Parra teaches a method for inferring the extent of European admixture in six different African-American populations [See Abstract]. In particular, Parra teaches a method for identifying a population structure by determining SNP markers for a first population using a battery of autosomal markers (both linked and unlinked) [See Abstract, and p.19-20, DNA Analysis Section, and Table 1]. Parra identifies allele frequencies corresponding to the 10 autosomal markers have frequencies differentials > 0.4 between one or more populations [Table 1, last column], which meets the claim language. The method requires standard PCR genotyping procedure, which inherently

requires contacting parent samples with markers [See p.20, Col. 1 and Table 1, last column]. In this population of markers, at least one is an autosomal polymorphism marker (D11S429) [p.20, Col. 1, and Table 1] that is associated with ancestry [Table 5], which shows the use at least one autosomal SNP that may be correlated but not linked to a gene-trait. A combination of SNP markers are selected to obtain an estimate of admixture for a sub-population [p.21, Col. 1, ¶ 2, and Fig. 1], wherein allele frequencies of the SNP markers are > 1% [Table 1], which is a teaching for minor allele frequencies. Parra shows the use of markers that are unlinked to certain loci [p.20, Col. 1, and p.23, Col. 2]. Parra calculates the frequency differences between populations based on SNPs [p.23, Col. 2]. The admixture distribution of the non-parental test populations is inferred within a predetermined confidence interval [p. 21 and Table 2]. Parra also shows fitting genotype frequencies to Hardy-Weinberg proportions and suggest the selection of genetic markers that show homogeneity with Africa and Europe based on allele frequency [p.20, Statistical Analysis]. Parra discloses a biogeographical ancestry trait (BGA) [Fig. 1], and admixture proportions of samples estimated using maximum likelihood calculations [p.20, Col. 2, ¶2 and ¶3]. Parra shows proportional ancestry comprising a three-way comparison of sub-populations of African-Americans and the distribution percentage of European alleles within this sub-population [Fig. 1] derived from maximum-likelihood methods [p.25, Col. 2]. Parra shows SNPs detected in a subpopulation of non-parental individuals for determining sub-population structure [Fig. 1].

Parra does not teach a first population of SNPs identified from a database in silico, as in claim 1.

Parra does not teach selecting SNPs from a first population to generate a second population of SNPs wherein the at least one SNP of the second population of SNPs have minor allele frequencies >1% and are not located within a region of a gene encoding a protein, as in claim 1.

Cargill teaches a method for screening samples to determine whether identified SNPs are coding or non-coding SNPs using well known genotyping techniques [p.232-233, Results, Table 1, and Table 2]. The method includes collecting gene sequence data from known public databases and suggests construction of comprehensive SNP databases to improve screening [See p. 237, Methods and p.236, Col. 1st paragraph]. Cargill also determines the distribution of minor allele frequency, wherein SNPs are classified according to whether minor allele frequency is high (>15%), medium (5-15%), or low (<1%) [p.234, Col. 1, last ¶, and Col. 2, and Fig. 1], which meets the claim limitation of minor allele frequencies > 1%.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Parra by selecting a first population of SNPs identified from a database in silico, as in claim 1, since Parra suggests genetic markers are easily obtained [p.20, Col. 1] and since Cargill shows computations methods for collecting gene sequence data from known public databases and suggests construction of comprehensive SNP databases [See p. 237, Methods and p.236, Col. 1st paragraph]. The motivation would have been to improve screening genotyping analysis by using

comprehensive databases containing data from many ethnic groups, as suggested by Cargill [p.236, Col. 1st paragraph].

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Parra by screening the first population of SNPs to generate a second population of SNPs wherein the at least one SNP of the second population of SNPs is not located within a region of a gene encoding a protein, as in claim 1, since Cargill shows screening genetic samples to determine whether identified SNPs are coding or non-coding SNPs that occur outside of the coding regions of a gene [p.232-233, Results, Table 1, and Table 2]. The motivation would have been to obtain the most informative SNP markers by screening the set of identified SNPs for non-coding SNPs which are known to effect biological function [Cargill, p.236, Col. 1, last paragraph].

Claims 1, 84-97, 99-100, and 104-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parra et al. (Am. J. Physical Antropol., January 2001, Vol. 114, Issue 1, p. 18-29), in view of Cargill et al. (Nature Genetics, 1999, Vol. 22, p.231-238), and further in view of Sorenson et al. (US 2003/0172065; Filed Mar. 29, 2002).

Parra and Cargill make obvious the method of claims 1, 84-86, 90-97, 99-100, and 104-109, as set forth above.

Parra and Cargill do not specifically teach contacting samples with high numbers of SNPs, as in claims 87- 89.

Parra and Cargill do not teach proportional ancestries comprising a photo of a person from whom the known proportional ancestry was determined, as in claims 110-115.

Sorenson discloses a genealogical research and record keeping system for identifying commonalities in haplotypes from biological samples [Abstract]. In particular, Sorenson teaches thousands of known genetic markers and millions of characterized SNPs may be analyzed [0042], [Fig. 4] for identifying a population structure [0032, 0046-0047], as in claim 87-89. Sorenson also discloses prior art genetic records of human eye, hair and skin color, height and other physical characteristics [0009], and ancestral data stored on microfiche and on a number of other electronic media formats including the internet [0003], which is broadly interpreted as a teaching for digital information and pictures as in claims 110-115.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method made obvious by Parra and Cargill by additionally contacting samples with high numbers of SNPs as in claims 87- 89, since Sorenson teaches genetic analysis using thousands of known genetic markers and millions of characterized SNPs [0042, Fig. 4]. The motivation would have been to address the need for correlating genetic information with genealogical information to identify previously unknown biological relationships or previous family ties, as suggested by as suggested by Sorenson [0013, 0015].

It would further have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method made obvious by Parra and Cargill by using

proportional ancestries comprising a photo of a person from whom the known proportional ancestry was determined, as in claims 110-115, since Sorenson teaches genetic records and ancestral data stored on microfiche and in electronic media format [0003, 0009]. The motivation would have been to improve the sharing of ancestral data using electronic formats that are suitable for the internet, as suggested by Sorenson [0003].

Claims 1, 84-101, and 104-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parra et al. (Am. J. Physical Antropol., January 2001, Vol. 114, Issue 1, p. 18-29), in view of Cargill et al. (Nature Genetics, 1999, Vol. 22, p.231-238), in view of Sorenson et al. (US 2003/0172065; Filed Mar. 29, 2002), and further in view of Shriver et al. (American Journal of Human Genetics, 1997, Vol. 60, p.957-964; IDS filed 5/20/2004).

Parra, Cargill, and Sorenson make obvious the method of claims 1, 84-97, 99-100, and 104-115, as set forth above. Parra also shows two-way and three-way comparison of populations that are both intracontinental and intercontinental [Table 1, Fig. 1, and p. 22].

Parra, Cargill, and Sorenson do not teach performing a likelihood determination for affiliation with an East Asian ancestral group, as in claim 98.

Parra, Cargill, and Sorenson do not teach performing four-way comparisons, as in claim 101.

Shriver teaches a method for identifying a set of genetic markers using likelihood analysis that allows the confident determination of ethnicity for use in a forensic setting [Abstract and p.964, Discussion]. In particular, Shriver presents population specific alleles (PSAs) [p.957, Col. 2], as well as methods for calculating allele-frequency differentials between test samples of different populations [p.958, Col. 2] and for calculating likelihood values for different loci [Table 1, and Table 2]. Shriver does not specifically teach "four-way" comparison. However, Shriver performs two-way and three-way comparisons between multiple populations [Fig. 1-4] and suggests similar markers could be developed for the identification of other populations including those of Asian origin [p.963, last ¶, Col. 1].

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method made obvious by Parra, Cargill, and Sorenson by performing a likelihood determination for affiliation with an East Asian ancestral group as required by claims 98, since Shriver identifies genetic markers using likelihood analysis [Abstract and p.964, Discussion, Table 1, and Table 2] and suggests markers for those of Asian ancestry [p.963, last ¶, Col. 1]. The motivation would have been to allow for the confident determination of ethnicity in forensic settings, as suggested by Shriver [Abstract and p.964, Discussion, Table 1, and Table 2].

It would further have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method made obvious by Parra, Cargill, and Sorenson by performing four-way comparisons, as in claim 101, since Parra and Shriver show performing two-way and three-way comparisons between multiple populations, as

set forth above. The motivation would have been to identify other populations that share common ancestry, as suggested by Shriver [p.963, Col. 1, last ¶, and Col. 2].

Claims 1 and 84-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parra et al. (Am. J. Physical Antropol., January 2001, Vol. 114, Issue 1, p. 18-29), in view of Cargill et al. (Nature Genetics, 1999, Vol. 22, p.231-238), in view of Sorenson et al. (US 2003/0172065; Filed Mar. 29, 2002), in view of Shriver et al. (American Journal of Human Genetics, 1997, Vol. 60, p.957-964; IDS filed 5/20/2004), and further in view of Pritchard et al. (Theoretical Population Biology, 2001, Vol. 60, p. 227-237).

Parra, Cargill, Sorenson, and Shriver make obvious the method of claims 1, 84-101, and 104-115, as set forth above.

Parra, Cargill, Sorenson, and Shriver do not teach generating a graphical representation of the comparison of three ancestral groups, wherein the representation comprises a confidence contour, as in claims 102 and 103.

Pritchard teaches a method for inferring proportional ancestry of different ancestral groups in a population structure using a graphical display format [Fig. 1], as in claims 102 and 103. Points in the extreme corners of the triangular plots are correctly classified [Fig. 1], which shows groups represented in a vertex of a triangle. Ancestry is also represented using a line plot, wherein dashed lines represent individuals from a population with the most divergent allele frequencies [Fig. 1 and p.232, Col. 2], which suggests a contour indicating a level of confidence. Pritchard also teaches a computer-

based program STRUCTURE for estimating population structure for 20 data sets of 50, 200, and 1000 biallelic markers [p. 232, Results].

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to practice the method made obvious by Parra, Cargill, Sorenson, and Shriver by generating a graphical representation, as in claims 102 and 103, since Pritchard shows graphically displaying ancestral results in triangular format [Fig. 1]. The motivation would have been to use a user-friendly graphical method for inferring ancestry in a plurality of populations, as suggested by Pritchard [Fig. 1].

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached between 12pm-8pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

Patent Examiner

Art Unit 1631

/PW/

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Supervisory Patent Examiner, Art Unit 1631